## REMARKS

## SUMMARY OF THE INVENTION

Applicants' invention is directed, *inter alia*, to polynucleotides encoding polypeptides having strong homology to canine C5a anaphylatoxin receptor (Perret, J.J., et al., (1992) Biochem. J., 288:911-917) ("CALR") and compositions containing them, which have a variety of utilities, in the diagnosis of conditions or diseases characterized by expression of CALR and for drug discovery (see the Specification at, e.g., page 6, line 15 through page 7, line 1; page 9, lines 13-22). As described in the Specification:

> The novel C5a-like receptor (CALR) which is the subject of this patent application was identified among the cDNAs derived from a mast cell library. Incyte Clone No. 8118 is a novel nucleotide sequence which is more closely related to CFCOMC5AM, the C5a anaphylatoxin receptor from dog (Perret JJ et al (1992) Biochem J 288:911-17) than to the known human C5a receptor. (Specification, page 2, lines 8-12.)

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> The present invention provides a unique nucleotide sequence identifying a novel C5a-like receptor which was first identified in human mast cells. The sequence for calr is shown in SEQ ID No 1 and is homologous to the GenBank sequence, CFCOMC5AM for canine C5a anaphylatoxin receptor. Incyte 8118 has 45% amino acid identity with the C5a receptor and differs from it in having only three carboxylate residues in the N-terminus, two of which are Glu rather than Asp. In addition, the N-terminus of Incyte 8118 is shorter than that of the published C5a receptor and would be expected to have different binding specificity.
>
> Because CALR is specifically expressed in cells active in immunity, the nucleic acid (calr), polypeptide (CALR) and antibodies to CALR are useful in investigations of and interventions in the normal and abnormal physiologic and pathologic processes which comprise the mast cell's role in immunity. Therefore, an assay for upregulated expression of CALR can accelerate diagnosis and proper treatment of conditions caused by abnormal signal transduction due to anaphylactic or hypersensitive responses, systemic and local infections, traumatic and other tissue damage, hereditary or environmental diseases associated with hypertension, carcinomas, and other physiologic or pathologic problems. (Specification, page 6, lines 7-22.)

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> The cDNA (SEQ ID NO 1) and amino acid (SEQ ID NO 2) sequences for human CALR are shown in Fig 1. Incyte's calr produced a BLAST score of 412 when compared with the C5a receptor sequence and has a probability of $1.8^{-50}$ that the sequence similarity occured by chance. This calr homolog also resembles various N-formylpeptide receptors generating BLAST scores ranging from 381 to 363 with probabilities of $7.4^{-46}$ to $3.2^{-43}$. When the translation of CALR was searched against protein databases such as SwissProt and PIR, no exact matches were found. Fig 2 shows the comparison of the human calr sequence with that of the dog C5a receptor, CFOMC5AM. (Specification, page 16, line 29 through page 17, line 1.)

Claims 12-17 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, based on the allegation that the claimed invention lacks patentable utility. The rejection alleges in particular that the invention has "no apparent or disclosed specific and substantial credible utility." (Office Action, page 2.)

**The rejection of claims 12-17 is improper, as the inventions of those claims have a patentable utility as set forth in the instant specification, and/or a utility well known to one of ordinary skill in the art.**

The invention at issue is a polynucleotide sequence corresponding to a gene that is expressed in a human mast cell library established from the peripheral blood of a patient with mast cell leukemia. The novel polynucleotide codes for a polypeptide demonstrated in the patent specification to be a member of the class of C5a-like seven transmembrane receptors, whose biological functions include binding complement and activating the immune function of mast cells. (Specification, e.g., at page 1, line 3 through page 3, line 16; page 6, lines 7-14; page 16, line 29 through page 17, line 1.) As such, the claimed invention has numerous practical, beneficial uses in drug development, and the diagnosis of disease. As a result of the benefits of these uses, the claimed invention already enjoys significant commercial success.

The Patent Examiner contends that the claimed polynucleotide cannot be useful without precise knowledge of its biological function. But the law never has required knowledge of biological function to prove utility. It is the claimed invention's uses, not its functions, that are the subject of a proper analysis under the utility requirement.

## I. The Applicable Legal Standard

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end"). *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. *See Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not make any showing to demonstrate utility. Manual of Patent Examination Procedure at §706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

## II. The uses of polynucleotides encoding CALR for diagnosis of conditions or diseases characterized by expression of CALR and for drug discovery are sufficient utilities under 35 U.S.C. §§ 101 and 112, first paragraph

The claimed invention meets all of the necessary requirements for establishing a credible utility under the Patent Law: There are "well-established" uses for the claimed invention known to persons of ordinary skill in the art, and there are specific practical and beneficial uses for the invention disclosed in the patent application's specification. Objective evidence, not considered by the Patent Office, further corroborates the credibility of the asserted utilities.

### A. The uses of polynucleotides encoding CALR for disease diagnosis are practical uses that confer "specific benefits" to the public

The claimed invention has specific, substantial, real-world utility by virtue of its use in disease diagnosis through gene expression profiling. There is no dispute that the claimed invention is in fact a useful tool in hybridization analysis used to perform gene expression

analysis. That is sufficient to establish utility for the claimed polynucleotide.

Nowhere does the Patent Examiner address the fact that, as described on page 6, line 15 through page 7, line 1, and page 9, lines 13-22 of the Specification, the claimed polynucleotides can be used as highly specific hybridization probes in, for example, northerns – probes that without question can be used to measure both the existence and amount of complementary RNA sequences known to be the expression products of the claimed polynucleotides. The claimed invention is not, in that regard, some random sequence whose value as a probe is speculative or would require further research to determine.

Given the fact that the claimed polynucleotide is known to be expressed, its utility as a measuring and analyzing instrument for expression levels is as indisputable as a scale's utility for measuring weight. This use as a measuring tool, regardless of how the expression level data ultimately would be used by a person of ordinary skill in the art, by itself demonstrates that the claimed invention provides an identifiable, real-world benefit that meets the utility requirement. *Raytheon* v. *Roper*, 724 F.2d 951, (Fed. Cir. 1983) (claimed invention need only meet one of its stated objectives to be useful); *In re Cortwright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999) (how the invention works is irrelevant to utility); MPEP § 2107 ("Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific, and unquestionable utility (e.g., they are useful in analyzing compounds)" (emphasis added)).

Though Applicants need not so prove to demonstrate utility, there can be no reasonable dispute that persons of ordinary skill in the art have numerous uses for information about relative gene expression including, for example, understanding the effects of a potential drug for treating mast cell-associated immune conditions caused by abnormal signal transduction due to anaphylactic or hypersensitive responses, systemic and local infections, traumatic and other tissue damage, hereditary or environmental diseases associated with hypertension, carcinomas, and other physiologic or pathologic problems. In other words, the person of ordinary skill in the art can derive more information about a potential mast cell-associated immune condition drug candidate or potential toxin with the claimed invention than without it.

**B. The use of nucleic acids coding for proteins expressed by humans as tools for drug discovery and the diagnosis of disease is now "well-established"**

The technologies made possible by expression profiling and the DNA tools upon which they rely are now well-established. The technical literature recognizes not only the prevalence of these technologies, but also their unprecedented advantages in drug development, testing and safety assessment.

Perret J.J. et al. (1992; Biochem J. 288:911-17; IDS Reference No. 6, incorporated by reference into the instant application; Reference No. 1) state that "[u]ltimately, the availability of the cloned receptors should help the design of pharmacologically active (non-peptide) inhibitors that could be used in syndromes were [*sic*: where] inappropriate complement activation occurs." (Perret, page 917.) The Specification discusses using the polynucleotides in "in production of chimeric molecules for selecting agonists, inhibitors or antagonists for design of domain-specific therapeutic molecules." (Specification, page 6, lines 27-29.) In addition the Specification describes the use of polypeptides encoded by the claimed polynucleotides in drug screening, for example, page 23, line 12 through page 24, line 14.

Because the Patent Examiner failed to address or consider the "well-established" utilities for the claimed invention in drug development, and the diagnosis of disease, the Examiner's rejections should be withdrawn regardless of their merit.

### C. The similarity of the polypeptide encoded by the claimed invention to another polypeptide of undisputed utility, as well as the expression of the CALR polypeptide in human mast cells, demonstrates utility

The Examiner alleged that "[t]he instant claims are drawn to a protein of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion the [*sic*: that] a protein of the instant invention is associated in any way with the plurality of causally unrelated disorders that are listed on page 6 of the instant specification." (Office Action, page 3.)

Applicants submit that there is adequate evidence in the Specification, along with what is well known in the art, to provide a "line of reasoning" to support the asserted utility for the claimed polynucleotide. This evidence is provided by not only sequence identity between CALR and canine C5a anaphylatoxin receptor but also the expression of CALR in human mast cells.

The utility of the claimed polynucleotide can be imputed based on the relationship

between the polypeptide it encodes, CALR, and another polypeptide of unquestioned utility, canine C5a anaphylatoxin receptor. The two polypeptides have sufficient similarities in their sequences that a person of ordinary skill in the art would recognize more than a reasonable probability that the polypeptide encoded for by the claimed invention has utility similar to canine C5a anaphylatoxin receptor. Applicants need not show any more to demonstrate utility. *In re Brana*, 51 F.3d at 1567.

It is undisputed, and readily apparent from the patent application, that the polypeptide encoded for by the claimed polynucleotide shares 46% sequence identity over 152 amino acid residues (L14 through T165 of CALR) with canine C5a anaphylatoxin receptor. This is more than enough homology to demonstrate a reasonable probability that the utility of canine C5a anaphylatoxin receptor can be imputed to the claimed invention (through the polypeptide it encodes). It is well-known that the probability that two unrelated polypeptides share more than 40% sequence homology over 70 amino acid residues is exceedingly small. Brenner et al., Proc. Natl. Acad. Sci. 95:6073-78 (1998) (Reference No. 2). Given homology in excess of 40% over many more than 70 amino acid residues, the probability that the polypeptide encoded for by the claimed polynucleotide is related to canine C5a anaphylatoxin receptor is, accordingly, very high.

The Examiner must accept the Applicants' demonstration that the homology between the polypeptide encoded for by the claimed invention and canine C5a anaphylatoxin receptor demonstrates utility by a reasonable probability unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility. See *In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). The Examiner has not provided sufficient evidence or sound scientific reasoning to the contrary.

Furthermore, confirmation of Applicants' identification of CALR as a human complement receptor is provided in Ames, R.S. et al. (1996; J. Biol. Chem., 271:20231-20334; "Molecular Cloning and Characterization of the Human Anaphylatoxin C3a Receptor"; Reference No. 3), in which the authors describe a human anaphylatoxin C3a receptor that has 98% sequence similarity to CALR.

As discussed *supra*, Perret et al. (Reference No. 1) describe how the availability of the cloned receptors of this family are useful in drug screening.

In addition the Specification describes how polynucleotides encoding CALR are

expressed in human mast cells as well as the importance of mast cells in immune response. The Specification teaches that human mast cells have "an important role in promoting various immune responses and nonspecific inflammatory reactions" and "degranulate and discharge granule contents extracellularly," and further that:

> Mast cell granule contents include histamine, heparin, elastase, cathepsin G, eosinophil chemotactic factors, platelet activating factor, and slow-reacting substance of anaphylaxis. When complement cleavage products 3a, 4a, and 5a bind to their respective receptors on the surface of mast cells and basophils, they are capable of triggering the release of histamine and the other factors without the involvement of IgE. Some of the factors listed above are synthesized by mast cells during the course of hypersensitivity reactions and mediate vaso- and broncho-constriction leading to asthma. These and other mediators released following degranulation are responsible both for allergy symptoms and for immunity against some parasites. (Specification, pages 2-3.)

The human mast cell line in which the claimed polynucleotide is expressed "was established from the peripheral blood of a Mayo Clinic patient with mast cell leukemia." (Specification, page 3.) The canine C5a receptor is "present on neutrophils, macrophages, and mast cells." (Specification, page 1, lines 9-10.)

This disclosure provides adequate support for a "line of reasoning" linking the diseases listed on page 6 of the Specification with the claimed polynucleotide. One of skill in the art would reasonably believe that a receptor, expressed in human mast cells and highly similar to a canine C5a receptor, has utility at least in diagnosis and treatment of mast cell-associated immune conditions.

Therefore, for at least the above reasons, the Specification provides adequate support for the asserted utility of the claimed polynucleotide.

**D. Objective evidence corroborates the utilities of the claimed invention**

There is, in fact, no restriction on the kinds of evidence a Patent Examiner may consider in determining whether a "real-world" utility exists. Indeed, "real-world" evidence, such as evidence showing actual use or commercial success of the invention, can demonstrate conclusive proof of utility. *Raytheon v. Roper*, 220 USPQ2d 592 (Fed. Cir. 1983); *Nestle v. Eugene*, 55 F.2d 854, 856, 12 USPQ 335 (6th Cir. 1932). Indeed, proof that the invention is made, used or sold by any person or entity other than the patentee is conclusive proof of utility. *United States*

*Steel Corp.* v. *Phillips Petroleum Co.*, 865 F.2d 1247, 1252, 9 USPQ2d 1461 (Fed. Cir. 1989).

Over the past several years, a vibrant market has developed for databases containing all expressed genes (along with the polypeptide translations of those genes), in particular genes having medical and pharmaceutical significance such as the instant sequence. (Note that the value in these databases is enhanced by their completeness, but each sequence in them is independently valuable.) The databases sold by Applicants' assignee, Incyte, include exactly the kinds of information made possible by the claimed invention, such as tissue and disease associations. Incyte sells its database containing the claimed sequence and millions of other sequences throughout the scientific community, including to pharmaceutical companies who use the information to develop new pharmaceuticals.

Both Incyte's customers and the scientific community have acknowledged that Incyte's databases have proven to be valuable in, for example, the identification and development of drug candidates. As Incyte adds information to its databases, including the information that can be generated only as a result of Incyte's discovery of the claimed polynucleotide and its use of that polynucleotide on cDNA microarrays, the databases become even more powerful tools. Thus the claimed invention adds more than incremental benefit to the drug discovery and development process.

## III. The Patent Examiner's Rejections Are Without Merit

Rather than responding to the evidence demonstrating utility, the Examiner attempts to dismiss it altogether by arguing that the disclosed and well-established utilities for the claimed polynucleotide are not "specific and substantial credible" utilities. (Office Action, page 2.) The Examiner is incorrect both as a matter of law and as a matter of fact.

### A. The Precise Biological Role Or Function Of An Expressed Polynucleotide Is Not Required To Demonstrate Utility

The Patent Examiner's primary rejection of the claimed invention is based on the ground that, without information as to the precise "biological role" of the claimed invention, the claimed invention's utility is not sufficiently specific.

It may be that specific and substantial interpretations and detailed information on

biological function are necessary to satisfy the requirements for publication in some technical journals, but they are not necessary to satisfy the requirements for obtaining a United States patent. The relevant question is not, as the Examiner would have it, whether it is known how or why the invention works, *In re Cortwright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999), but rather whether the invention provides an "identifiable benefit" in presently available form. *Juicy Whip Inc.* v. *Orange Bang Inc.*, 185 F.3d 1364, 1366 (Fed. Cir. 1999). If the benefit exists, and there is a substantial likelihood the invention provides the benefit, it is useful. There can be no doubt that the present invention meets this test.

The threshold for determining whether an invention produces an identifiable benefit is low. *Juicy Whip*, 185 F.3d at 1366. Only those utilities that are so nebulous that a person of ordinary skill in the art would not know how to achieve an identifiable benefit and, at least according to the PTO guidelines, so-called "throwaway" utilities that are not directed to a person of ordinary skill in the art at all, do not meet the statutory requirement of utility. Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

Knowledge of the biological function or role of a biological molecule has never been required to show real-world benefit. In its most recent explanation of its own utility guidelines, the PTO acknowledged so much (66 F.R. at 1095):

> [T]he utility of a claimed DNA does not necessarily depend on the function of the encoded gene product. A claimed DNA may have specific and substantial utility because, *e.g.*, it hybridizes near a disease-associated gene or it has gene-regulating activity.

By implicitly requiring knowledge of biological function for any claimed nucleic acid, the Examiner has, contrary to law, elevated what is at most an evidentiary factor into an absolute requirement of utility. Rather than looking to the biological role or function of the claimed invention, the Examiner should have looked first to the benefits it is alleged to provide.

### B. Membership in a Class of Useful Products Can Be Proof of Utility

Despite the uncontradicted evidence that the claimed polynucleotide encodes a polypeptide in the C5a-like seven transmembrane receptor family, the Examiner refused to impute the utility of the members of the C5a-like seven transmembrane receptor family to CALR. In the Office Action, the Patent Examiner takes the position that, unless Applicants can

identify which particular biological function within the class of C5a-like seven transmembrane receptors is possessed by CALR, utility cannot be imputed. To demonstrate utility by membership in the class of C5a-like seven transmembrane receptors, the Examiner would require that all C5a-like seven transmembrane receptors possess a "common" utility.

There is no such requirement in the law. In order to demonstrate utility by membership in a class, the law requires only that the class not contain a substantial number of useless members. So long as the class does not contain a substantial number of useless members, there is sufficient likelihood that the claimed invention will have utility, and a rejection under 35 U.S.C. § 101 is improper. That is true regardless of how the claimed invention ultimately is used and whether or not the members of the class possess one utility or many. *See Brenner* v. *Manson*, 383 U.S. 519, 532 (1966); *Application of Kirk*, 376 F.2d 936, 943 (CCPA 1967).

Membership in a "general" class is insufficient to demonstrate utility only if the class contains a sufficient number of useless members such that a person of ordinary skill in the art could not impute utility by a substantial likelihood. There would be, in that case, a substantial likelihood that the claimed invention is one of the useless members of the class. In the few cases in which class membership did not prove utility by substantial likelihood, the classes did in fact include predominately useless members. *E.g.*, *Brenner* (man-made steroids); *Kirk* (same); *Natta* (man-made polyethylene polymers).

The Examiner addresses CALR as if the general class in which it is included is not the C5a-like seven transmembrane receptor family, but rather all polynucleotides or all polypeptides, including the vast majority of useless theoretical molecules not occurring in nature, and thus not pre-selected by nature to be useful. While these "general classes" may contain a substantial number of useless members, the C5a-like seven transmembrane receptor family does not. The C5a-like seven transmembrane receptors family is sufficiently specific to rule out any reasonable possibility that CALR would not also be useful like the other members of the family.

Because the Examiner has not presented any evidence that the C5a-like class of seven transmembrane receptors has any, let alone a substantial number, of useless members, the Examiner must conclude that there is a "substantial likelihood" that the CALR encoded by the claimed polynucleotide is useful. It follows that the claimed polynucleotide also is useful.

Even if the Examiner's "common utility" criterion were correct – and it is not – the C5a-

like seven transmembrane receptor family would meet it. It is undisputed that known members of the C5a-like seven transmembrane receptor family are seven transmembrane receptors that bind complement and activate the immune function of mast cells. A person of ordinary skill in the art need not know any more about how the claimed invention binds complement and activates the immune function of mast cells to use it, and the Examiner presents no evidence to the contrary. Instead, the Examiner makes the conclusory observation that a person of ordinary skill in the art would need to know whether, for example, any given C5a-like seven transmembrane receptors binds complement and activates the immune function of mast cells. The Examiner then goes on to assume that the only use for CALR absent knowledge as to how the C5a-like seven transmembrane receptor actually works is further study of CALR itself.

Not so. As demonstrated by Applicants, knowledge that CALR is a C5a-like seven transmembrane receptor is more than sufficient to make it useful for the diagnosis and treatment of mast cell-associated immune conditions. Indeed, CALR has been shown to be expressed in mast cells. The Examiner must accept these facts to be true unless the Examiner can provide evidence or sound scientific reasoning to the contrary. But the Examiner has not done so.

### C. Because the uses of polynucleotides encoding CALR in drug discovery, and disease diagnosis are practical uses beyond mere study of the invention itself, the claimed invention has substantial utility.

As used in drug discovery and disease diagnosis, the claimed invention has a beneficial use in research other than studying the claimed invention or its protein products. It is a tool, rather than an object, of research. The data generated in gene expression monitoring using the claimed invention as a tool is not used merely to study the claimed polynucleotide itself, but rather to study properties of tissues, cells, and potential drug candidates and toxins. Without the claimed invention, the information regarding the properties of tissues, cells, drug candidates and toxins is less complete.

The claimed invention has numerous additional uses as a research tool, each of which alone is a "substantial utility." These include uses in chromosomal mapping (Specification, page 9, line 23 through page 10, line 6.)

## IV. By Requiring the Patent Applicant to Assert a Particular or Unique Utility, the Patent Examination Utility Guidelines and Training Materials Applied by the

**Patent Examiner Misstate the Law**

There is an additional, independent reason to withdraw the rejections: to the extent the rejections are based on Revised Interim Utility Examination Guidelines (64 FR 71427, December 21, 1999), the final Utility Examination Guidelines (66 FR 1092, January 5, 2001) and/or the Revised Interim Utility Guidelines Training Materials (USPTO Website www.uspto.gov, March 1, 2000), the Guidelines and Training Materials are themselves inconsistent with the law.

The Training Materials, which direct the Examiners regarding how to apply the Utility Guidelines, address the issue of specificity with reference to two kinds of asserted utilities: "specific" utilities which meet the statutory requirements, and "general" utilities which do not. The Training Materials define a "specific utility" as follows:

> A [specific utility] is *specific* to the subject matter claimed. This contrasts to *general* utility that would be applicable to the broad class of invention. For example, a claim to a polynucleotide whose use is disclosed simply as "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

The Training Materials distinguish between "specific" and "general" utilities by assessing whether the asserted utility is sufficiently "particular," *i.e.*, unique (Training Materials at p.52) as compared to the "broad class of invention." (In this regard, the Training Materials appear to parallel the view set forth in Stephen G. Kunin, Written Description Guidelines and Utility Guidelines, 82 J.P.T.O.S. 77, 97 (Feb. 2000) ("With regard to the issue of specific utility the question to ask is whether or not a utility set forth in the specification is *particular* to the claimed invention.")).

Such "unique" or "particular" utilities never have been required by the law. To meet the utility requirement, the invention need only be "practically useful," *Natta*, 480 F.2d 1 at 1397, and confer a "specific benefit" on the public. *Brenner*, 383 U.S. at 534. Thus, incredible "throw-away" utilities, such as trying to "patent a transgenic mouse by saying it makes great snake food," do not meet this standard. Karen Hall, Genomic Warfare, The American Lawyer 68 (June 2000) (quoting John Doll, Chief of the Biotech Section of USPTO).

This does not preclude, however, a general utility, contrary to the statement in the

Training Materials where "specific utility" is defined (page 5). Practical real-world uses are not limited to uses that are unique to an invention. The law requires that the practical utility be "definite," not particular. *Montedison,* 664 F.2d at 375. Applicants are not aware of any court that has rejected an assertion of utility on the grounds that it is not "particular" or "unique" to the specific invention. Where courts have found utility to be too "general," it has been in those cases in which the asserted utility in the patent disclosure was not a practical use that conferred a specific benefit. That is, a person of ordinary skill in the art would have been left to guess as to how to benefit at all from the invention. In *Kirk,* for example, the CCPA held the assertion that a man-made steroid had "useful biological activity" was insufficient where there was no information in the specification as to how that biological activity could be practically used. *Kirk,* 376 F.2d at 941.

The fact that an invention can have a particular use does not provide a basis for requiring a particular use. *See Brana, supra* (disclosure describing a claimed antitumor compound as being homologous to an antitumor compound having activity against a "particular" type of cancer was determined to satisfy the specificity requirement). "Particularity" is not and never has been the *sine qua non* of utility; it is, at most, one of many factors to be considered.

As described *supra,* broad classes of inventions can satisfy the utility requirement so long as a person of ordinary skill in the art would understand how to achieve a practical benefit from knowledge of the class. Only classes that encompass a significant portion of nonuseful members would fail to meet the utility requirement. *Supra* § III.B. (*Montedison,* 664 F.2d at 374-75).

The Training Materials fail to distinguish between broad classes that convey information of practical utility and those that do not, lumping all of them into the latter, unpatentable category of "general" utilities. As a result, the Training Materials paint with too broad a brush. Rigorously applied, they would render unpatentable whole categories of inventions that heretofore have been considered to be patentable and that have indisputably benefitted the public, including the claimed invention. *See supra* § III.B. Thus the Training Materials cannot be applied consistently with the law.

## V. To the Extent the Rejection of the Patented Invention under 35 U.S.C. § 112, First Paragraph, Is Based on the Improper Rejection for Lack of Utility under 35 U.S.C. § 101, it Must Be Withdrawn.

The rejection set forth in the Office Action is based on the assertions discussed above, i.e., that the claimed invention lacks patentable utility. To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the same reasons.

## CONCLUSION

Applicants respectfully submit that rejections for lack of utility based, *inter alia*, on an allegation of "lack of specificity," as set forth in the Office Action and as justified in the Revised Interim and final Utility Guidelines and Training Materials, are not supported in the law. Neither are they scientifically correct, nor supported by any evidence or sound scientific reasoning. These rejections are alleged to be founded on facts in court cases such as *Brenner* and *Kirk*, yet those facts are clearly distinguishable from the facts of the instant application, and indeed most if not all nucleotide and protein sequence applications. Nevertheless, the PTO is attempting to mold the facts and holdings of these prior cases, "like a nose of wax,"[1] to target rejections of claims to polypeptide and polynucleotide sequences where biological activity information has not been proven by laboratory experimentation, and they have done so by ignoring perfectly acceptable utilities fully disclosed in the specification as well as well-established utilities known to those of skill in the art. As is disclosed in the specification, and even more clearly, as one of ordinary skill in the art would understand, the claimed invention has well-established, specific, substantial and credible utilities. The rejections are, therefore, improper and should be withdrawn.

Moreover, to the extent the above rejections were based on the Revised Interim and final Examination Guidelines and Training Materials, those portions of the Guidelines and Training Materials that form the basis for the rejections should be determined to be inconsistent with the law.

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[1]"The concept of patentable subject matter under §101 is not 'like a nose of wax which may be turned and twisted in any direction * * *.' *White v. Dunbar*, 119 U.S. 47, 51." *(Parker v. Flook,* 198 USPQ 193 (US SupCt 1978))

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent at (650) 845-4646.

Please charge Deposit Account No. **09-0108** in the amount of **$1004.00** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: January 25, 2002

Susan K. Sather

Susan K. Sather
Reg. No. 44,316
Direct Dial Telephone: (650) 845-4646

3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

## IN THE CLAIMS:

**Claims 18-22 have been added.**

**Claims 12, 13, 14, 15, and 17 have been amended as follows.**

12. (Once Amended) An isolated [and purified] polynucleotide comprising a polynucleotide sequence encoding the amino acid sequence of [shown in] SEQ ID NO:2.

13. (Once Amended) An isolated [and purified] polynucleotide comprising the polynucleotide sequence of [shown in] SEQ ID NO:1.

14. (Once Amended) An isolated [and purified] polynucleotide fully complementary to a polynucleotide comprising the polynucleotide [the] sequence of SEQ ID NO:1 [claim 13].

15. (Once Amended) An expression vector comprising the isolated [and purified] polynucleotide of claim 12.

17. (Once Amended) A method for producing a polypeptide comprising the amino acid sequence of [shown in] SEQ ID NO:2, said method comprising the steps of:

(a) culturing the host cell of claim 16 under conditions suitable for expression of the polypeptide, and

(b) recovering said polypeptide from the cell culture.